

REMARKS

General:

Claims 1 to 11 are pending in this application. Claims 1 to 11 stand rejected.

Enablement:

Claims 1 to 11 were rejected under 35 U.S.C. § 112, first paragraph, for lack of an enabling disclosure. First, the examiner states that there is a lack of enablement regarding “the predictability of convergence of the methodology ... as each trial structure is found.” It is respectfully submitted that the examiner has not made out a *prima facie* case for the rejection.

“According to *In re Bowen*, 492 F.2d 859, 862-63, 181 USPQ 48, 51 (CCPA 1974), the minimal requirement is for the examiner to give reasons for the uncertainty of the enablement. This standard is applicable even when there is no evidence in the record of operability without undue experimentation beyond the disclosed embodiments.” MPEP § 2164.05.

In the present case, the examiner has not shown that the enablement is uncertain. He has agreed that it is not known how certain the enablement is. The most that could possibly be said in support of the examiner’s position is that “there is no evidence in the record of operability without undue experimentation beyond the disclosed embodiments,” and that, as the above passage from the MPEP makes clear, is not a sufficient basis for an enablement rejection.

It is, of course, common general knowledge that an iterative optimization process will occasionally fail to find the global optimum solution although, as Kariuki remarks (page 189, right column, lines 6-8), “the genetic algorithm is often found to be superior to alternative approaches.” However, the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled. *Atlas Powder Co. v. E. I. duPont de Nemours & Co.*, 750 F.2d 1569, 224 U.S.P.Q. 409, 414 (Fed. Cir. 1984). There is no evidence that the failure rate of the present process is substantially greater than is usual for iterative optimization processes, so the degree of trial and error required will also not be substantially greater than is usual for iterative optimization processes. “The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation.” MPEP § 2164.01(a), citing to *In re Certain Limited-*

Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom, Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985).

In this context, it is respectfully pointed out that the person skilled in the art for the purposes of the present invention is a multidisciplinary team, consisting of a mathematician skilled in data processing and a crystallographer. As confirmation of this, the examiner is referred to the library cataloguing data on the background reading materials filed with this response, all of which are classified under "crystallography," "data processing," or "computer science." The excerpt from Young's book shows specifically that the idea of combining the mathematics of algorithmic optimization with crystallography was not new in 1997. The mathematician would have been familiar in 1997 with the inherent problems of iterative optimization processes, which had been well known for a long time. It is therefore submitted that the examiner has shown no more uncertainty and experimentation than "the art typically engages in," and reconsideration of the examiner's rejection is respectfully requested.

Second, the examiner states that there is a lack of enablement "regarding the determination of a predetermined fitness threshold." This rejection is stated in the form of a reference back to a previous office action, where the rejection is stated in the form of a further reference back. It is supposed that the examiner intends to reaffirm the rejection at page 3, lines 14-16 of the office action dated October 12, 2001 that the "predetermined threshold is not defined in the specification so as to enable the reader to reproduce it." The reader does not need to reproduce anything. The reader is told, see for example page 19, lines 26-29 of the original PCT text, that the function of the threshold is to identify as successful a set of values with a low calculated fitness, that is to say, with a low degree of difference from the real powder diffraction data that are the target. Subject to that function, the choice of threshold is essentially entirely discretionary. A higher threshold will result in a shorter process; a lower threshold will result in a more precise final result, and less risk of a local optimum result that is not the global optimum result.

One of the major advantages of the process of the present invention is that using a reduced dataset for the calculations greatly increases the speed of the process. It is therefore

entirely feasible, with the present invention, to set a very low threshold and simply leave the computer to run. As shown in Figures 6 and 7b, a few thousand generations may be sufficient and, with the process of the present invention and the computers available in 1997, that took hours, rather than the days or weeks to which crystallographers were accustomed.

It is respectfully submitted that no valid ground of rejection has been shown, and reconsideration is requested.

Third, claims 1 to 4 and 6 to 11 were rejected under 35 U.S.C. § 112, first paragraph, on the ground that the specification "does not reasonably provide enablement for a generic fitness calculation." The examiner's argument, in so far as it can be understood, is predicated on applying the high degree of unpredictability that prevails in molecular biology (see page 6, lines 10 to 12 of the office action). By doing so, the examiner acknowledges that different arts have different degrees of uncertainty. "*In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity)." MPEP § 2164.03.

The examiner's only basis for importing the biological level of unpredictability is that the mathematical algorithm of the present invention "may be applied to molecules including those of biological origin" and that the structures of some biological molecules are highly uncertain. With respect, this is not a sufficient basis. The method of the present invention is essentially an analytical technique. An analytical technique does not become unpredictable merely because it is applied to unpredictable, or totally unknown, subject matter. Most analytical techniques used in the real world will occasionally return an incorrect or inconclusive result, but that does not mean the technique itself is uncertain or unpredictable.

Further, by the examiner's own admission, the algorithm may also be applied to subjects that are not biological molecules, so the lower unpredictability of arts other than molecular biology applies with equal logic. Thus, the origin of the subject crystal cannot provide a proper basis for assessing the unpredictability of the mathematics, because it cannot provide a consistent basis. It is therefore submitted that the normal reputation of

mathematics as the most exact of all sciences must prevail, and with it the correspondingly low degree of unpredictability.

The examiner argues that "a fitness calculation is reasonably a detailed knowledge area which may be generally known but not necessarily specifically well known for a specific invention area" (page 8, lines 9-12 of the office action). However, as explained above, the skilled person for the present purpose is a team including a mathematician who would understand fitness calculations and a crystallographer who would know what parts of the data are important. Between the two of them, they would be able to apply the general concept of fitness calculations to the specific area of crystal diffraction.

For all of the above reasons, the examiner's rejection is therefore respectfully traversed.

As far as applicants' attorneys can determine, the part of the office action from page 5, line 4 to page 13, line 11, headed "Response to arguments regarding various lack of enablement rejections" does not state any further ground of rejection, but is directed solely to discussion in support of the rejections noted above, and in reply to applicants' earlier arguments. If any distinct ground of rejection was intended to have been raised, in those pages, it is respectfully requested that the ground be re-stated.

The examiner rejects the background documents filed with the applicants' last response on the sole ground that they do not bear dates of publication earlier than the filing date of the present application. Background documents with dates before the date of filing of the application are filed herewith. To verify the dates of publication, both British Library and Library of Congress catalog records are included for each publication. It is noted that some of the documents supplied concerned subjects (such as the chi-squared test) so old that there is no reason to suppose that the knowledge in the art had changed between the filing of the present application in 1998 and the downloading of the web pages in 2002. The examiner is also referred to the Kariuki paper, which was filed and reviewed just after applicants' priority date. Of course Kariuki was not examined under 35 USC § 112, but there is a reasonable inference that Kariuki, and the reviewers at Chemical Physics Letters,

expected it to be understood by the skilled reader. What Kariuki does not explain, he implies was already known as of October 1997.

The examiner was informed at the time that the earlier documents were delayed in the transatlantic mails and that the undated materials had been filed as an interim measure. Applicants' attorneys did offer to file the dated documents when they were received, but the examiner at that time declined the offer, apparently on the ground that he believed the extra volume of paper to be unnecessary.

The examiner's attention is drawn in particular to Michalewicz, who provides a methodology for handling multimodal optimization in case the use of multiple diffraction data sets does produce "conflicting results ... wherein evaluation confusion will occur." Also, Von Dreele's paper in Young specifically discusses an iterative process using both X-ray and neutron diffraction data.

35 U.S.C. § 102:

Claims 1 and 6 to 11 are rejected as anticipated by Kariuki et al. Kariuki et al. bears a date of publication of December 5, 1997. The present application claims priority under 35 U.S.C. § 119(a)-(d) from an application filed in the United Kingdom on July 31, 1997. The claim to priority was made in the original PCT Request, affirmed in the Declaration filed in the present application on April 18, 2000, and acknowledged in the filing receipt issued on May 1, 2000. A certified copy of the foreign application has been received by the U.S. Patent Office, as acknowledged in the Notification of Acceptance of Application dated April 27, 2000. The applicants' claim to priority is therefore believed to have been perfected. Applicants believe and assert that claims 1 and 6 to 11 are supported by the foreign application, and are entitled to the priority date of July 31, 1997. That priority date is before the effective date of the reference, and the rejection is traversed.

Textual informality:

The clerical error in claim 1 is corrected by the present amendment.

Conclusion:

In view of the foregoing, reconsideration of the examiner's rejections and objections and allowance of all of claims 1 to 11 are earnestly solicited.

Respectfully submitted,

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